

32. The method according to claim 5 wherein the plant or plant part is an agricultural or horticultural plant.

33. The method according to claim 32 wherein the agricultural or horticultural plant is selected from the group consisting of *Malus*, *Pyrus*, *Vita*, *Citrus*, *Lycopersicon*, *Brassica*, *Persea*, *Copernicia*, *Ceroxylon*, and *Eriobotrya*.

34. The method of claim 5 wherein the plant or plant part is *Malus*.

35. The method of claim 5 wherein the plant or plant part is *Lycopersicon*.

36. The method of claim 5 wherein the plant or plant part is exposed to a solvent for a brief period of time.

37. The method of claim 36 wherein the plant or plant part is exposed to a solvent from about three minutes to about five minutes.

38. The method of claim 37 wherein the plant or plant part is exposed to a room temperature solvent.

39. The method of claim 5 wherein the plant or plant part is fruit peel.--

REMARKS

The Applicants would like to thank the Examiner for the courtesy extended on September 24, 2001, in that the Examiner agreed to disregard the paper filed on September 10, 2001, which was styled as a preliminary amendment, but was in fact filed after the first Official Action was mailed. Timely receipt of all future office communications concerning this application is now expected, as a power of attorney appointing the undersigned attorney and other practitioners at his firm has been entered.

Claims 5-10 were pending in this application prior to the present amendment. By the foregoing amendment, claims 5, 8 and 9 have been amended, and dependent claims

19-39 have been added. Enclosed herewith is a check to cover the filing fee of \$172 for nineteen additional total claims in excess of twenty, paid at the small entity rate to which Applicants are entitled. No new matter has been added. Accordingly, claims 5-10, and 19-39 are now pending. Pursuant to 37 C.F.R. §1.121, a marked-up version of the changes made to the claims by the present amendment is attached hereto as Exhibit A, following the signature page of this amendment. Exhibit A is captioned "Version With Markings to Show Changes Made." Also attached hereto, as Exhibit B, is a list of all claims that will be pending upon entry of the instant amendment.

In the outstanding Official Action, claims 5-7 and 9-10 were rejected under 35 U.S.C. 102(b) as being anticipated by U.S. Patent No. 4,594,412 to Kitagawa (hereinafter "Kitagawa") or U.S. Patent No. 5,130,133 to Rajagopalan *et al.* (hereinafter "Rajagopalan"). Additionally, claims 5-10 were rejected under 35 U.S.C. 103(a) as being unpatentable over Rajagopalan, or alternatively over Kitagawa (Applicants assume that claims 1-5 were not examined as set forth in this rejection).

In an Official Action mailed on June 29, 2001, the Examiner set forth a restriction requirement advising that if Group I (including claim 2) was elected, the Applicants must identify a single disclosed species from those listed in claim 2. Group I was not elected in the Applicants' response to the restriction requirement. However, new claim 24 includes all of the species that are listed in claim 2. Applicants assert that a similar requirement is inappropriate with respect to the method claims that have been elected for prosecution because such methods can be practiced with a variety of plant species. However, to expedite prosecution, the Applicants provisionally elect *Malus*, in anticipation of a corresponding restriction requirement being applied against new claim 24.

Moreover, although Applicants maintain that analogous requirements to elect a single species in claims 27, 29, 31, and 33 would be improper, in order to expedite prosecution, Applicants provisionally elect *Malus* in claims 27, 31 and 33, and *Copernicia* or *Ceroxylon* (wax palm) in claim 29, if a similar requirement is imposed.

Reconsideration of the application, in light of the present amendment and the following remarks is solicited.

The various bases for the claim rejections will be addressed below in the order raised in the Official Action.

Claim Rejections - 35 U.S.C. § 102(a)

The Applicants respectfully traverse the rejection of claims 5-7 and 9-10 as anticipated by Kitagawa or Rajagopalan.

In rejecting claims 5-7 and 9-10, the Examiner stated that it was known in the art that the outer membranes of plants and plant parts were mainly composed of higher chain alkyls such as lipids and waxes, and that these materials were removed easily via exposure to non-polar solvents such as hexanes and ether. The Examiner further asserted that while Rajagopalan and Kitagawa are silent with regard to whether the compositions possess anti-viral activity, the compositions must inherently possess anti-viral activity because the method steps are the same.

It is respectfully submitted that the Examiner is applying an incorrect standard for anticipation. Anticipation arises where a single prior art reference discloses a claimed invention such that a skilled artisan could take its teachings in combination with his own knowledge of the particular art and be in possession of the claimed invention. *In re Graves*, 69 F.3d 1147, 1152 (Fed. Cir. 1995). Applicants respectfully submit that Rajagopalan and Kitagawa fail to disclose, suggest, or appreciate a method for producing a preparation possessing antiviral activity comprising substances obtained from cuticular or epicuticular layers of a plant or plant part, and therefore do not anticipate the claimed methods. These patents simply disclose defatting plant tissues to remove undesirable constituents.

It is well-established that each and every limitation of a claimed invention must be present in a single prior art reference in order for anticipation to occur. *See*, for example, *C.R. Bard, Inc. v. M3 Systems, Inc.*, 157 F.3d 1340, 1349 (Fed. Cir. 1998). The standard is one of strict identity. This standard has not been satisfied for the reasons set forth in more detail, below.

Furthermore, claim 5 has been amended to more clearly set forth the nature of Applicants' invention, which relates to Applicants' discovery that antiviral compounds may be isolated from the epicuticular and cuticular layer of plants and plant parts while

leaving the internal epidermis substantially intact. Accordingly, in the methods according to the invention, there is essentially no disruption of plant cells interior to the epidermal layer.

Rajagopalan discloses two methods for extracting fatty constituents from plant tissue. *See generally*, Rajagopalan at column 4, lines 35-62. In both methods, substantial disruption of the plant cells interior to the epidermal layer occurs. For example, according to the first method the fatty constituents are extracted "using an extraction apparatus where the solvent is refluxed through the tissues for a long period of time." *See* Rajagopalan at column 4, lines 57-59. According to the second method, fatty constituents are extracted from plant tissues by blending the solvent and material together. *See* Rajagopalan at column 4, lines 44-45. More specifically, according to the second method, Rajagopalan discloses the use of a 3-speed blender with a speed of 18,000 rpm for extracting the material. *See* Rajagopalan, Example 10.

Accordingly, Rajagopalan does not disclose or suggest a method wherein the plant or plant part is exposed to a solvent under conditions sufficient to solubilize materials in the cuticular and epicuticular layers of the plant, while leaving cells and tissues internal to the epidermis substantially unaffected. Accordingly, Rajagopalan does not anticipate claim 5 or any of the claims depending therefrom.

Kitagawa also discloses defatting plant tissues to remove undesirable fatty constituents from the plant tissue, presumably to simplify the purification of the desired components. "The defatting is effected with an ordinary fat-soluble organic solvent such as ether, hexane, benzene, petroleum ether, ligroin, ethyl acetate or the like, usually under heating." *See* Kitagawa at column 2, lines 46-49. More specifically, Kitagawa discloses defatting by heating plant tissue under reflux. *See* Kitagawa, Examples 1-7. Further, in addition to heating the plant tissue to reflux, Kitagawa preferentially pulverizes or cuts the tissue to be extracted. *See* Kitagawa at column 2, lines 40-41 and Examples 1-7. Accordingly, Kitagawa does not disclose or suggest a method wherein the plant or plant part is exposed to a solvent under conditions sufficient to solubilize materials in the cuticular and epicuticular layers of the plant, while leaving cells and tissues internal to the epidermis substantially unaffected. Thus, Kitagawa does not anticipate any of claims 5-7 or 9-10 or any other of the pending claims.

Further, it is respectfully submitted that neither Rajagopalan nor Kitagawa discloses or suggests a method for producing a preparation possessing antiviral activity comprising substances obtained from cuticular or epicuticular layers of a plant or plant part. Accordingly, the anticipation rejection is improper because there is no disclosure of producing an antiviral preparation, as required by all of the pending claims.

Nonetheless, in the Official Action, the Examiner has asserted that because the method steps are the same, the products are the same. As set forth above, Applicants respectfully submit that the method steps are not the same. Further, the Federal Circuit has established the proper criteria for anticipation rejections based on purported inherency.

“Inherency . . . may not be established by probabilities or possibilities. The mere fact that a certain thing may result from a given set of circumstances is not sufficient. If, however, the disclosure is sufficient to show that the natural result flowing from the operation as taught would result in the performance of the questioned function, it seems to be well settled that the disclosure should be regarded as sufficient.”
Mehl/Biophile Int'l Corp. v. Milgraum, 192 F.3d 1362, 1365 (Fed. Cir. 1999) (quoting *In re Oelrich*, 666 F.2d 578, 581 (C.C.P.A. 1981))

Nothing in the Examiner's rejection, however, provides factual support that the method of defatting plant tissues disclosed by Rajagopalan and/or Kitagawa would produce an antiviral preparation, thereby reducing the basis for the Examiner's rejection to one of probability or possibility. Moreover, under the doctrine of inherent anticipation, one of ordinary skill must recognize that the methods of Rajagopalan and/or Kitagawa inevitably produce antiviral preparations, and there is no evidence to establish that required fact. Accordingly, Applicants submit that the rejection is improper and must therefore be withdrawn.

Claim Rejections - 35 U.S.C. § 103(a)

The Applicants respectfully traverse the rejection of claims 5-10 as being unpatentably obvious under § 103(a) over Rajagopalan, or alternatively over Kitagawa.

Applicants respectfully submit that the cited references actually teach away from the claimed invention. As the Examiner has recognized, neither reference discloses or suggests an antiviral activity for the outer lipid (fatty/waxy) layer; the references simply

disclose the removal of the outer lipid (fatty/waxy) layer of the leaves prior to further processing steps. Accordingly, there is no disclosure, suggestion or appreciation in the cited references of any utility for the compounds derived from the epicuticular and cuticular layers.

Section 2141.02 of the M.P.E.P. states that "A prior art reference must be considered in its entirety, *i.e.*, as a whole, including portions that would lead away from the claimed invention." Applicants respectfully submit that it is improper to use a reference which specifically teaches away from the claimed invention as support for an obviousness rejection. Accordingly, the rejection of claims 5-10 under 35 U.S.C. § 103(a) over Rajagopalan or, alternatively, over Kitagawa, has been overcome and may properly be withdrawn.

It is submitted that the application is now in condition for allowance and an early notice thereof is respectfully solicited. If the Examiner has any question or would like to discuss the matters addressed herein further, the Examiner is invited to contact the undersigned representative at the telephone number indicated below.

Respectfully submitted,

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December 21, 2001



EXHIBIT A

VERSION WITH MARKINGS TO SHOW CHANGES MADE

In the Claims:

Claims 5, 8 and 9 have been amended as follows:

5.(Amended) A method for producing a preparation possessing antiviral activity comprising substances obtained from cuticular or epicuticular layers of a plant or plant part, the method comprising:

a) exposing the plant or plant part to a solvent under conditions sufficient to solubilize materials in the cuticular and epicuticular layers of the plant, while leaving cells and tissues internal to the epidermis substantially unaffected [, thereby]; and

b) obtaining a solution or suspension of plant cuticular and epicuticular materials, [and, optionally, b) removing the solvent,] thereby producing the antiviral preparation.

8. (Amended) The method of claim 5 wherein the step of exposing [comprising] comprises spraying the plant or plant part with the solvent.

9. (Amended) The method of claim [9] 19 wherein the removal of the solvent is performed by a method selected from the group consisting of aspiration, static evaporation, heating, centrifugal evaporation, rotary evaporation, vortex evaporation, lyophilization, liquid-liquid separation, solid-liquid separation and precipitation.

EXHIBIT B

PENDING CLAIMS

5. (Amended) A method for producing a preparation possessing antiviral activity comprising substances obtained from cuticular or epicuticular layers of a plant or plant part, the method comprising:

a) exposing the plant or plant part to a solvent under conditions sufficient to solubilize materials in the cuticular and epicuticular layers of the plant, while leaving cells and tissues internal to the epidermis substantially unaffected; and

b) obtaining a solution or suspension of plant cuticular and epicuticular materials, thereby producing the antiviral preparation wherein the antiviral activity is selected from the group consisting of an anti-human immunodeficiency virus activity, an anti-herpesvirus activity, an anti-influenza virus activity, an anti-rhinovirus activity, an anti-poliovirus activity, an anti-hepadnavirus activity, an anti-cytomegalovirus activity, an anti-measles virus activity, an anti-parainfluenza virus activity, an anti-vesicular stomatitis virus activity, an anti-vaccinia virus activity, an anti-encephalitis virus activity and an anti-African Swine Fever virus activity and the plant or plant part is selected from the group consisting of *Malus*, *Pyrus*, *Vita*, *Citrus*, *Lycopersicon*, *Brassica*, *Cucumis*, *Prunus*, *Persea*, *Vaccinium*, *Arctostaphylos*, *Olea*, *Nicotianum*, *Quercus*, *Eucalyptus*, *Rhododendron*, *Ilex*, *Eriobotrya*, *Salix*, *Copernicia*, *Euphorbia*, *Pedilanthus*, *Syagrus*, *Cocos*, *Attalea*, *Stipa*, *Glyceria*, *Saccharum*, *Myrica*, *Rhus*, *Sapium*, *Ceroxylon*, *Linum*, *Agave*, *Cannabis*, *Raphia*, *Coccus*, *Ligustrum*, *Fraxinus*, *Benincasa*, *Ricinus*, *Buxus*, *Mesembryanthemum*, *Rubus* and *Melaleuca*.

6. The method of claim 5 wherein the solvent comprises one or more ingredients selected from the group consisting of hexane, chloroform, dichloromethane, heptane, ether, petrolether, t-butyl ether, DMSO, supercritical fluids and carbon dioxide.

7. The method of claim 5 wherein the step of exposing comprises dipping the plant or plant part into the solvent.

8. The method of claim 5 wherein the step of exposing comprises spraying the plant or plant part with the solvent.
9. The method of claim 19 wherein the removal of the solvent is performed by a method selected from the group consisting of aspiration, static evaporation, heating, centrifugal evaporation, rotary evaporation, vortex evaporation, lyophilization, liquid-liquid separation, solid-liquid separation and precipitation.
10. An antiviral preparation prepared by the method of claim 5.
19. The method according to claim 5 further comprising removing the solvent.
20. The method according to claim 19 further comprising redissolving the antiviral preparation in a biologically compatible medium.
21. The method according to claim 5 further comprising clarifying the solution or suspension of plant cuticular and epicuticular materials.
22. The method according to claim 5 further comprising formulating the antiviral preparation into a pharmaceutical composition.
23. The method according to claim 5 further comprising formulating the antiviral preparation into a nutraceutical composition.
24. The method according to claim 5 wherein the plant or plant part is selected from the group consisting of *Malus*, *Pyrus*, *Vita*, *Citrus*, *Lycopersicon*, *Brassica*, *Cucumis*, *Prunus*, *Persea*, *Vaccinium*, *Arctostaphylos*, *Olea*, *Nicotianum*, *Quercus*, *Eucalyptus*, *Rhododendron*, *Ilex*, *Eriobotrya*, *Salix*, *Copernicia*, *Euphorbia*, *Pedilanthus*, *Syagrus*, *Cocos*, *Attalea*, *Stipa*, *Glyceria*, *Saccharum*, *Myrica*, *Rhus*, *Sapium*, *Ceroxylon*, *Linum*, *Agave*, *Cannabis*, *Raphia*, *Coccus*, *Ligustrum*, *Fraxinus*, *Benincasa*, *Ricinus*, *Buxus*, *Mesembryanthemum*, *Rubus* and *Melaleuca*.

25. The method according to claim 5 wherein the antiviral activity is selected from the group consisting of an anti-human immunodeficiency virus activity, an anti-herpesvirus activity, an anti-influenza virus activity, an anti-rhinovirus activity, an anti-poliovirus activity, an anti-hepadnavirus activity, an anti-cytomegalovirus activity, an anti-measles virus activity, an anti-parainfluenza virus activity, an anti-vesicular stomatitis virus activity, an anti-vaccinia virus activity, an anti-encephalitis virus activity and an anti-African Swine Fever virus activity.

26. The method according to claim 5 wherein the anti-herpesvirus activity is anti-HSV activity.

27. The method according to claim 26 wherein the plant or plant part is selected from the group consisting of *Malus*, *Pyrus*, *Vita*, *Citrus*, *Lycopersicon*, *Prunus*, *Eriobotrya*, *Copernicia*, *Ceroxylon* and *Persea*.

28. The method according to claim 5 wherein the antiviral activity is anti-HIV activity.

29. The method according to claim 28 wherein the plant or plant part is selected from the group consisting of *Prunus*, *Eriobotrya*, *Copernicia*, *Ceroxylon* and *Salix*.

30. The method according to claim 5 wherein the antiviral activity is anti-influenza activity.

31. The method according to claim 30 wherein the plant or plant part is selected from the group consisting of *Malus*, *Lycopersicon*, *Brassica* and *Persea*.

32. The method according to claim 5 wherein the plant or plant part is an agricultural or horticultural plant.

33. The method according to claim 32 wherein the agricultural or horticultural plant is selected from the group consisting of *Malus*, *Pyrus*, *Vita*, *Citrus*, *Lycopersicon*, *Brassica*, *Persea*, *Copernicia*, *Ceroxylon*, and *Eriobotrya*.

34. The method of claim 5 wherein the plant or plant part is *Malus*.

35. The method of claim 5 wherein the plant or plant part is *Lycopersicon*.

36. The method of claim 5 wherein the plant or plant part is exposed to a solvent for a brief period of time.

37. The method of claim 36 wherein the plant or plant part is exposed to a solvent from about three minutes to about five minutes.

38. The method of claim 37 wherein the plant or plant part is exposed to a room temperature solvent.

39. The method of claim 5 wherein the plant or plant part is fruit peel.